digested DNA and three fragments (approximately sized at 3.7kb, 10.5kb and 13kb) on EcoRI digested DNA.

Please replace the paragraph beginning at page 8, line 10, with the following rewritten paragraph:

Figure 7. Sequence of human CLASP-5 exons and introns, and promoter. **A)** Sequence of human CLASP-5 exons and intron borders (SEQ ID NOS:64-85). Stretches of noncontiguous genomic sequence from the Human Genome Project (Genbank entry gi10045359) were aligned using the human CLASP-5 cDNA as a template and Sequencher sequence analysis software. Due to the incompleteness of the Human Genome Project, only partial genomic sequence from human CLASP-5 was obtained. 22 exons representing approximately the 5' 40% of the human CLASP-5 cDNA sequence are presented in predicted 5' to 3' order. Exon sequences are underlined and are flanked by intron sequence. This exon/intron map could only have been produced having the isolated human CLASP-5 cDNA. Nucleotide numbers in parentheses refer to the exon sequence within the uniquely-generated, contiguous gi10045359 sequence, which is located **7B**. **B)** Ordered stretch of human genomic DNA at the CLASP-5 locus (SEQ ID NO:86) aligned from noncontiguous, shotgun sequencing from the Human Genome Project using the human CLASP-5 sequence from FIG. 6A to determine genomic DNA fragment order and orientation. **C)** Sequence of putative human CLASP-5 promoter (SEQ ID NO:87). The 5' terminus of the CLASP-5 cDNA is underlined. This sequence represents nucleotides 126774 to 128870 of Genbank entry gi10045359.

Please replace the paragraph beginning at page 8, line 27, with the

Figure 8. [illegible]

(h) CLASP family members (SEQ ID NO:88-93). Amino acid sequences were aligned

using ClustalW. The alignment is presented in order of their greatest pairwise similarity scores. Single letter amino acid abbreviations are used. Asterisks indicate complete identity, while colons and periods indicate sequence similarity among CLASP family members. Dashes indicate gaps inserted in the amino acid sequence to facilitate alignment. Labeled boxes are domains with similarity to known protein motifs; boxes represent regions of similarity between all CLASPs and may represent CLASP-specific domains.

Please replace the paragraph beginning at page 12, line 3, with the following rewritten paragraph:

The phrase "sequence similarity" in the context of two nucleic acids or polypeptides, refers to two or more sequences that are identical or in the case of amino acids, have homologous amino acid substitutions at either 50%, often at least 60%, often at least 70%, preferably at least 80%, most preferably at least 90% or at least 95% of the indicated positions.

Please replace the paragraph beginning at page 17, line 6, with the following rewritten paragraph:

Similarly, products of an immune response in either a model organism (*e.g.*, mouse) or a human patient can also be detected by various methods that are well known to those of ordinary skill in the art. For example, (1) the production of antibodies in response to vaccination can be readily detected by standard methods currently used in clinical laboratories, *e.g.*, an ELISA; (2) the migration of immune cells to sites of inflammation can be detected by scratching the surface of skin and placing a sterile

phagocytic capacity of granulocytes, macrophages, and other phagocytes in PBMC's can

be measured by placing PMBCs in wells together with labeled particles (Peters *et al.*, 1988), and (5) the differentiation of immune system cells can be measured by labeling PBMCs with antibodies to CD molecules such as CD4 and CD8 and measuring the fraction of the PBMCs expressing these markers.

Please replace the paragraph beginning at page 21, line 27, with the following rewritten paragraph:

The human CLASP-5 sequence presented in FIG. 6 encodes one potential start site for translation. The predicted methionine appears at nucleotide +1 (ATG). Due to the lack of in-frame stop codons upstream of the predicted initiator methionine in FIG. 6, a second possibility for a translational start is that the cDNA listed in FIG. 6 is incomplete and another methionine is encoded in frame and upstream of the sequence shown in FIG. 6.

Please replace the paragraph beginning at page 30, line 33, with the following rewritten paragraph:

Standard assays can be used for detecting CLASP protein interaction with cytoskeletal proteins. These assays include co-sedimentation assays, far western blot analysis (Ohba, T., 1998, Anal. Biochem. 262: 185-192), surface pasman resonance, F-actin staining with phalloidin in CLASP-transfected lymphocytes (*e.g.*, Small, J. *et al.* 1999, Microsc. Res. Tech. 4: 3-17), and immunocytol analysis of subcellular distribution of focal adhesion proteins (such as paxillin, tensin, vinculin, talin, and FAK in CLASP-transfected lymphocytes; see, *e.g.*, Ridyard, M.S., 1998, Biochem. Cell Biol. 76: 45-58).

Please replace the paragraph beginning at page 32, line 17, with the

As illustrated in FIG. 5, CLASP-5 has motifs found in a superfamily of immune-cell associated proteins with similar motifs (e.g., CLASP-1, 2, 6, 3, 4, 5, 7).

CLASP-1 is described in WO 00/20434. CLASP-1 uniquely among the known CLASPs contains SH3 binding domain motifs. CLASP-2 is described in WO 00/61747. CLASP 2 polypeptides have no adaptor binding sites or SH3 binding domains found in CLASP-1. Other CLASP family members are described in Application Nos. 09/736,960; 09/736,969; 09/737,246 (Attorney Docket Nos. 020054-000311US, 020054-000411US, 020054-000611US) (all filed December 13, 2000), 60/240,508, 60/240,503, 60/240,539, and 60/240,543 (all filed October 13, 2000). The aforementioned publications and applications are all incorporated by reference herein in its entirely for all purposes.

Please replace the paragraph beginning at page 32, line 17, with the following rewritten paragraph:

In one embodiment, the CLASP-5 polynucleotide is identical or exactly complementary to SEQ ID NO:1 or selectively hybridizes to an aforementioned sequence. In various embodiments, the polynucleotide is identical or exactly complementary to, or selectively hybridizes to, the nucleotide sequence encoding a particular protein domain or region, or a particular gene exon of the CLASP-5 mRNA or genomic sequence. Such polynucleotides are particularly useful as probes, because they can be selected to identify a defined species of CLASP-5.

Please replace the paragraph beginning at page 35, line 33, with the following rewritten paragraph:

In some embodiments, the CLASP-5 polynucleotides of the invention are substantially identical to SEQ ID NO:1 or to a fragment thereof.

Please replace the paragraph beginning at page 36, line 28, with the

"Stringent hybridization conditions" are conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acid.

but not to other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen, Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Probes, "Overview of principles of hybridization and the strategy of nucleic acid assays" (1993). Generally, stringent conditions are selected to be about 5-10°C lower than the thermal melting point (Tm) for the specific sequence at a defined ionic strength pH. The Tm is the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at Tm, 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (*e.g.*, 10 to 50 nucleotides) and at least about 60°C for long probes (*e.g.*, greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For high stringency hybridization, a positive signal is at least two times background, preferably 10 times background hybridization. Exemplary high stringency or stringent hybridization conditions include: 50% formamide, 5x SSC and 1% SDS incubated at 42° C or 5x SSC and 1% SDS incubated at 65° C, with a wash in 0.2x SSC and 0.1% SDS at 65° C. In a specific embodiment, a nucleic acid which is hybridizable to a CLASP-5 nucleic acid under the following conditions of high stringency is provided: Prehybridization of filters containing DNA is carried out for 8 h to overnight at 65°C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 8-16 h at 65°C in solution containing 2X SSC, 0.1% SDS. This is followed by a wash in 0.2X SSC and

Please replace the paragraph beginning at page 41, line 4. with the following rewritten paragraph:

A variety of uses of the CLASP promoter sequence provided herein will be apparent to one of skill reviewing this disclosure. In an embodiment, reporter genes are operably linked to CLASP upstream sequences containing promoter elements. The resulting vectors have numerous uses, including identification of cis and trans transcriptional regulatory factors in vivo and for screening of agents capable of modulating (e.g., activating or inhibiting) CLASP expression (e.g., drug screening). In an embodiment, for example, a modulator of CLASP expression can be identified by detecting the effect of the modulator on expression of a reporter gene whose expression is regulated, in whole or part, by a naturally occurring CLASP regulatory element (e.g., promoter or enhancer). A number of reporters may be used (e.g., firefly luciferase, β-glucuronidase, β-galactosidase, chloramphenicol acetyl transferase, SEAP, GFP). In a related embodiment, a CLASP coding sequence is used in place of a reporter and changes in CLASP protein expression (or activity) is detected using the methods disclosed herein. In a related embodiment, the ability of a test compound to bind to a CLASP gene regulatory sequence is assayed.

Please replace the paragraph beginning at page 43, line 31, with the following rewritten paragraph:

Methods of selecting nucleic acid probe sequences for use in nucleic acid hybridization are discussed in Sambrook *et al.*, supra. In some formats, at least one of the target and probe is immobilized. The immobilized nucleic acid can be DNA, RNA, or another oligo- or poly-nucleotide, and can comprise natural or non-naturally occurring

oligonucleotide arrays (e.g., GeneChips™ Affymetrix, dip sticks, pins, chips, or beads). All of these techniques are well known in the art and are the basis of many commercially

available diagnostic kits. Hybridization techniques are generally described in Hames *et al.*, ed., 1985, Nucleic Acid Hybridization, A Practical Approach IRL Press; Gall and Pardue, 1969, Proc. Natl. Acad. Sci. U.S.A., 63: 378-383; and John *et al.*, 1969, Nature, 223: 582-587.

Please replace the paragraph beginning at page 47, line 21, with the following rewritten paragraph:

The presence or absence of hCLASP-5 nucleotide and amino acid sequences in a biological sample can be used in screening assays as medical diagnostics to aid in clinical decision-making. As discussed above, hCLASP-5 is expressed at high levels in peripheral blood leukocytes, in which hCLASP-5 is highly expressed. Therefore, in one embodiment, hCLASP-5-based diagnostics involves screening assays for the detection hCLASP-5 nucleotide and amino acid sequences in PBMCs. Detection can be achieved by standard assays known to one of skill in the art including quantitative RT-PCR, Northern analysis, Western analysis, flow cytometry/fluorescence-activated cell sorting (FACS), ELISA, immunofluorescence and immunoperoxidase staining using anti-hCLASP-5 antibodies (Sambrook, Fritsch and Maniatas, 1989, Molecular Cloning, 2nd Ed, Cold Spring Harbor Lab. Press; Harlow et. al. ,1988, Antibodies, a laboratory manual, Cold Spring Harbor Lab. Press). Detection of the presence or absence of elevated numbers of leukocytes in urine is useful for the diagnosis of infections of the urinary system. Current diagnostics screening assays routinely test urine for the presence of leukocyte esterase (Fauci et al Eds., Harrison's Principles of Internal Medicine, 14th Ed. McGraw Hill, 1998, pp. 817-22). Detection of hCLASP-5 would provide a viable alternative to current methods.

In another embodiment, hCLASP-5-based diagnostics involve screening assays for identifying disorders of cells of hematopoietic lineage. hCLASP-5 is expressed in myelomonocytes, promyelocytes and B cells but not in T cells or monocytes (figure 2B). Furthermore, promyelocytes use a different splice variant of hCLASP-5 and permit discrimination based on hCLASP-5 isoform to distinguish between promyelocytes and myelomonocytes or monocytes. The identification of precise hematopoietic cell lineage is vital to guide chemotherapy and radiation therapy of leukemias and lymphomas (Fauci et al., (eds.), 1998 Harrison's Principles of Internal Medicine, 14th Ed. McGraw Hill, pp. 695-712). hCLASP-5 provides an additional marker to classify more precisely the affected cells. hCLASP-5 expression differences can be detected, for example, by using FACS, immunofluorescence, immunoperoxidase staining, RT-PCR, in situ hybridization or RNA blot analysis (Sambrook, Fritsch and Maniatas, Molecular Cloning, 2nd Ed. Cold Spring Harbor Lab. Press, 1989; Ward MS, Pathology 1999 Nov; 31(4): 382-92).

Please replace the paragraph beginning at page 48, line 27, with the following rewritten paragraph:

In another embodiment, hCLASP-5-based diagnostics involve screening assays for identifying activated immune system cells. Although hCLASP-5 is generally expressed at high levels in PBMCs, it is known that the surface expression of the closely related mouse CLASP-1 protein is altered during the process of lymphocyte activation. An analogous change in expression is expected for the hCLASP-5 protein. Subtyping lymphocytes specific for a particular antigen, for example, using MHC-based multimeric staining reagents (Altman et. al., 1996, Science 274: 94-6), for separating cell populations into hCLASP-5 high and hCLASP-5 low populations, can aid in determining the nature

infections.

Please replace the paragraph beginning at page 50, line 16, with the following rewritten paragraph:

It will be appreciated that the CLASP-5 polynucleotides and oligonucleotides of the invention can be made using nonstandard bases (*e.g.*, other than adenine, cytidine, guanine, thymine, and uridine) or nonstandard backbone structures to provides desirable properties (*e.g.*, increased nuclease-resistance, tighter-binding, stability or a desired TM). Techniques for rendering oligonucleotides nuclease-resistant include those described in PCT publication WO 94/12633. A wide variety of useful modified oligonucleotides may be produced, including oligonucleotides having a peptide-nucleic acid (PNA) backbone (Nielsen *et al.*, 1991, Science 254: 1497) or incorporating 2'-O-methyl ribonucleotides, phosphorothioate nucleotides, methyl phosphonate nucleotides, phosphotriester nucleotides, phosphorothioate nucleotides, phosphoramidates. Still other useful oligonucleotides may contain alkyl and halogen-substituted sugar moieties comprising one of the following at the 2' position: OH, SH, SCH3, F, OCN, OCH3OCH3, OCH3O(CH2)nCH3, O(CH2)nNH2 or O(CH2)nCH3, where n is from 1 to about 10; C1 to C10 lower alkyl, substituted lower alkyl, alkaryl or aralkyl; Cl; Br; CN; CF3; OCF3; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; SOCH3 ; SO2CH3; ONO2; NO2; N3; NH2; heterocycloalkyl; heterocycloalkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a cholesteryl group; a folate group; a reporter group; an intercalator; a group for improving the pharmacokinetic properties of an oligonucleotide; or a group for improving the pharmacodynamic properties of an oligonucleotide and other substituents having similar properties. Folate, cholesterol or other groups that facilitate oligonucleotide uptake, such as lipid analogs, may be conjugated directly or via a linker at the 2' position of any

have sugar moieties such as cyclobutyls in place of the pentofuranosyl group. Other embodiments may include at least one modified base form or "universal base" such as

inosine, or inclusion of other nonstandard bases such as queosine and wybutosine as well as acetyl-, methyl-, thio- and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases. The antisense oligonucleotide can comprise at least one modified base moiety which is selected from the group including, but not limited to, 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5β-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine.

Please replace the paragraph beginning at page 53, line 33, with the following rewritten paragraph:

Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites which include the following sequences, GUA, GUU and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides corresponding to the region of the target gene containing the cleavage site can be evaluated for predicted structural features such

assays.

Please replace the paragraph beginning at page 64, line 3, with the following rewritten paragraph:

The present invention provides new antibacterial agents. Certain CLASP-5 DNA sequences were difficult to clone and subclone (*see* Example 1). Bacteria harboring certain pieces of CLASP cDNA products were unable to be isolated, indicating that introduction of CLASP sequences compromised bacterial viability. There can be at least two possible reasons why the CLASP cDNA were unable to be cloned, which can reflect a variation of the well-established Modification and Restriction systems found in bacteria (reviewed in Wilson and Murray. (1991) Annu. Rev. Genet. 25:585-627; Bickle and Kruger (1993) Microbiol. Rev. 57:29-67). This well-described system is used by bacteria to prevent deleterious effects caused by the introduction of foreign DNA. Bacteria can recognize foreign DNA since it does not have the same modifications (e.g. methylation) as the native DNA. After recognition, the bacteria then digest and eliminate the foreign DNA (restriction). In the first scenario, the CLASP cDNA can be recognized as foreign DNA, and digested and eliminated as in the Modification and Restriction system. However, this would be unique for CLASP cDNA since the bacteria used for cloning cDNA are compromised in the Modification and Restriction system, which makes cloning of cDNA into bacteria a practice common in the art. If this is the case, the bacterial apparatus that specifically recognizes or eliminates CLASP cDNA can provide a novel target to develop antimicrobial agents. The CLASP DNA sequence would be useful in targeting the apparatus as well as an entry point for designing screens to identify potential targets. The second possibility is that CLASP cDNA behaves as an antimicrobial agent (i.e., antibiotic), and prevents bacterial growth. This, in effect, would create a new type of antibiotic mediated by the presence of foreign DNA (i.e. variation of the restriction and prevent the bacteria from growing, imposing a bactericidal effect upon the bacteria.

Please replace the paragraph beginning at page 71, line 4, with the following rewritten paragraph:

In cases where plant expression vectors are used, the expression of the CLASP-5 coding sequence can be driven by any of a number of promoters. For example, viral promoters such as the 35S RNA and 19S RNA promoters of CaMV (Brisson *et al.*, 1984, Nature 310: 511-514), or the coat protein promoter of TMV (Takamatsu *et al.*, 1987, EMBO J. 6: 307-311) can be used; alternatively, plant promoters such as the small subunit of RUBISCO (Coruzzi *et al.*, 1984, EMBO J. 3: 1671-1680; Broglie *et al.*, 1984, Science 224: 838-843); or heat shock promoters, *e.g.*, soybean hsp17.5-E or hsp17.3-B (Gurley *et al.*, 1986, Mol. Cell. Biol. 6: 559-565) can be used. These constructs can be introduced into plant cells using Ti plasmids, Ri plasmids, plant virus vectors, direct DNA transformation, microinjection, electroporation, and the like. (Weissbach & Weissbach, 1988, Methods for Plant Molecular Biology, Academic Press, NY, Section VIII, pp. 421-463; and Grierson & Corey, 1988, Plant Molecular Biology, 2d Ed., Blackie, London, Ch. 7-9.).

Please replace the paragraph beginning at page 74, line 10, with the following rewritten paragraph:

In an alternate embodiment of the invention, the coding sequence of CLASP-5 could be synthesized in whole or in part, using chemical methods well known in the art. (See, *e.g.*, Caruthers *et al.*, 1980, Nuc. Acids Res. Symp. Ser. 7: 215-233; Crea and Horn, 180, Nuc. Acids Res. 9(10): 2331; Matteucci and Caruthers, 1980, Tetrahedron Letter 21: 719; and Chow and Kempe, 1981, Nuc. Acids Res. 9(12): 2807-2817.) Alternatively, the protein itself could be produced using chemical methods to synthesize

high performance liquid chromatography. (See Creighton, 1983, Proteins Structures And Molecular Principles, W.H. Freeman and Co., N.Y. pp. 50-60). The composition of the

synthetic polypeptides can be confirmed by amino acid analysis or sequencing (*e.g.*, the Edman degradation procedure, see Creighton, 1983, Proteins, Structures and Molecular Principles, W.H. Freeman and Co., N.Y., pp. 34-49).

Please replace the paragraph beginning at page 80, line 23, with the following rewritten paragraph:

Various procedures known in the art can be used for the production of antibodies to epitopes of the natural and recombinantly produced CLASP-5 protein. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, human or humanized, IgG, IgM, IgA, IgD or IgE, a complementarity determining region, Fab fragments, F(ab')2 and fragments produced by an Fab expression library as well as anti-idiotypic antibodies. Antibodies which compete for CLASP-5 binding are especially preferred for diagnostics and therapeutics.

Please replace the paragraph beginning at page 81, line 8, with the following rewritten paragraph:

For the production of antibodies, various host animals can be immunized by injection with the recombinant or naturally purified CLASP-5 protein, fusion protein or peptides, including but not limited to goats, rabbits, mice, rats, hamsters, and the like Various adjuvants can be used to increase the immunological response, depending on the host species, including but not limited to Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, dinitrophenol, and potentially useful human adjuvants such as BCG (bacilli Calmette-Guerin) and

following rewritten paragraph:

Monoclonal antibodies to CLASP-5 can be prepared by using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique originally described by Kohler and Milstein, (Nature, 1975, 256: 495-497), the human B-cell hybridoma technique (Kosbor *et al.*, 1983, Immunology Today, 4: 72; Cote *et al.*, 1983, Proc. Natl. Acad. Sci. U.S.A., 80: 2026-2030) and the EBV-hybridoma technique (Cole *et al.*, 1985, Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc., pp. 77-96). In addition, techniques developed for the production of "chimeric antibodies" (Morrison *et al.*, 1984, Proc. Natl. Acad. Sci. U.S.A., 81: 6851-6855; Neuberger *et al.*, 1984, Nature, 312: 604-608; Takeda *et al.*, 1985, Nature, 314: 452-454) by splicing the genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. Alternatively, techniques described for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce CLASP-5 -specific single chain antibodies. In some embodiments, phage display technology is used to identify antibodies and heteromeric Fab fragments that specifically bind to selected antigens (see, *e.g.*, McCafferty *et al.*, Nature 348: 552-554 (1990); Marks *et al.*, Biotechnology 10: 779-783 (1992)).

Please replace the paragraph beginning at page 84, line 15, with the following rewritten paragraph:

CLASP-5 activities include, for example, the CLASP-5 polypeptide involvement in signal transduction (*e.g.*, leading to T cell activation). Compounds or agents that modulate the interaction of a CLASP-5 polypeptide and a target molecule,

Please replace the paragraph beginning at page 87, line 24, with the following rewritten paragraph:

Typically, the assays are recombinant cell based or cell-free assay. These assays can include the steps of combining a cell expressing a CLASP-5 polypeptide or a binding fragment thereof, a CLASP-5 target molecule (*e.g.*, a CLASP-5 ligand) and a test compound, under conditions where but for the presence of the candidate compound, the CLASP-5 polypeptide or biologically active portion thereof binds to the target molecule. Detecting complex formation between the CLASP-5 polypeptide or the binding fragment thereof, the CLASP-5 target molecule and a test compound detecting the formation of a complex which includes the CLASP-5 polypeptide and the target molecule can be accomplished. Detection of complex formation can include direct quantitation of the complex by, for example, measuring inductive effects, such as T cell activation, of the CLASP-5 polypeptide. A significant change, such as a decrease, in the interaction of the CLASP-5 and target molecule (*e.g.*, in the formation of a complex between the CLASP-5 and the target molecule) in the presence of a candidate compound (relative to what is detected in the absence of the candidate compound) is indicative of a modulation of the interaction between the CLASP-5 polypeptide and the target molecule. Modulation of the formation of complexes between the CLASP-5 polypeptide and the target molecule can be quantitated using, for example, an immunoassay. To perform cell free drug screening assays, it is desirable to immobilize either CLASP-5 or its target molecule to facilitate separation of complexes from uncomplexed forms of one or both of the polypeptides, as well as to accommodate automation of the assay. CLASP-5 binding to a target molecule, in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for containing the reactants. Examples of such vessels include microtitre plates, test tubes, and microcentrifuge tubes.

Please replace the paragraph beginning at page 99, line 30, with the

rejection is ectopic heart transplantation (Ulmer *et al.*, 1963, Am. J. Anat. 113: 273-281).

transplanting cardiac tissue into a surgically-created pocket on the dorsum for both ears made by slitting the skin over the auricular artery at the base of the ear. Small curved forceps are forced into the slit, bluntly dissecting between the skin and the cartilage plate. Donor tissue is eased into the base of the pocket near the distal edge of the ear. The auricular artery is used to seal off the opening of the pocket. Within 10 to 14 days pulsatile activity of the transplant should be observed. Gross appearance of the graft, patterns of vacuolar supply to the graft area and pulsatile activity can be easily observed utilizing transilluminated light during the first three weeks post-transplantation. Follow-up can continue for several months.

Please replace the paragraph beginning at page 100, line 17, with the following rewritten paragraph:

Once a titer of the potency of collagen type II (CII) is obtained therapeutics can be tested. In one embodiment, three mice will be immunized with three different concentrations of CII 50, 200, and 400 μg per animal (Nabozny *et al.*, 1996, J. Exp. Med., 183: 27-37). To induce CIA, animals can be immunized with an appropriate concentration of CII, determined as described above. One half of a 1:1 ratio of antigen:CFA can be injected at the base of the tail and the remainder equally divided in each hind footpad. Mice can be carefully monitored every day for the onset and progression of CIA throughout the experiment until its termination 12 weeks post-immunization with CII. The pieces of heart transplanted can be approximately 3 X 3 mm in size. The severity of arthritis can be assessed following standard procedures known to one of skill in the art.

Please replace the line beginning at page 101, line 29, with the following

Please replace the paragraph beginning at page 103, line 2, with the following rewritten paragraph:

Cell supernatants harvested after cell stimulation for 16-48 hrs are stored at -80°C until assayed or directly tested for cytokine production. Multiple cytokine assays can be performed on each sample. IL-2, IL-3, IFN-γ and other cytokine ELISA Assays are available for mouse, rat, and human (Endogen, Inc. and BioSource). Cytokine production is measured using a standard two-antibody sandwich ELISA protocol as described by the manufacturer. The presence of horseradish peroxidase is detected with 3, 3'5, 5' tertamethyl benziidine (TMB) substrate and the reaction is stopped with sulfuric acid. The absorbency at 450 nm is measured using a microplate reader. Any statistically significant increase or decrease in color intensity of CLASP-5-treated sample, as compared to control sample (no treatment), suggest an effect of CLASP-5 on biological function.

Please replace the line beginning at page 104, line 30, with the following line:

(M) Structure/Function Assays: Homotypic and/or Heterotypic, Calcium-dependent Cell Adhesion

Please replace the paragraph beginning at page 106, line 27, with the following rewritten paragraph:

To obtain additional 5' CLASP-5 sequence, portions of the cDNA and genomic sequence from a BAC (Bacterial Artificial Chromosome) genomic library were compared to the NCBI database by BLAST. A genomic clone (Genbank identifier: gi|AL161725 comprising random, shotgun genomic sequence was identified. Using TFASTX (Pearson and Lipman, PNAS (1988) 85:2444-2448), the amino-terminal

[illegible] reverse transcriptase polymerase chain reaction according to manufacturers instructions:

Reverse transcriptase Gibco/BRL, Taq Polymerase from Sigma). Using oligonucleotides HC5gS1 (nucleotides 1498-1519 of FIG. 6) and oligonucleotide HC5AS10b (reverse complement of nucleotides 3642-3660 of FIG. 6) a RTPCR product of approximately 3.0 kb was generated, sequenced (dideoxynucleotide termination sequencing, Beckman Coulter CEQ2000) and shown to be additional human CLASP-5 5' sequence. Further complicating the cloning full-length CLASP cDNA products was the difficulty to clone (and subclone) certain CLASP cDNA products. Standard isolation of some of the CLASP cDNAs from a pure phage population following screening of commercially available cDNA libraries ("ZAP-out" procedure, Stratagene) resulted in no bacterial colonies. Similarly, certain RT-PCR products could not be cloned into standard plasmid vectors. No colonies were isolated by cloning these fragments into vectors lacking promoters, reverse orientations, low copy vectors, or by growth at altered temperatures or levels of antibiotic for plasmid selection (examples: CLASP-7 - HC7gS6 to HC7gAS1 and HC7gS3 to HC7AS14; CLASP-4 – C4P2 to hC4ASTM and C4P2 to HC4AS3'; CLASP-1 – hC1S5' to hC1AS3'Kpn and C1S7 to hC1AS3'Kpn; see Primer Table below). One possibility is that sequences contained within certain regions of CLASP cDNAs are bacteriacidal and therefore not amenable to cloning. To circumvent these problems direct sequencing of RT-PCR products was performed.

Please replace the paragraph beginning at page 108, line 14, with the following rewritten paragraph:

RACE was carried out using Invitrogen's Generacer kit according to manufacturers specifications using polyA selected mRNA from 9D10 B cell tissue culture line. The sequence of the oligonucleotides presented is the reverse complement

Please replace the paragraph beginning at page 108, line 26, with the following rewritten paragraph:

Clones (GI:10045359, GI:9944141) have previously been mapped to the chromosomal location 9p24.3. The literature research reports that the mutations, deletions, rearrangements, disomies and/or breakpoints (in general: chromosomal aberrations) in below listed genes make the genes strong candidates for the onset of the listed disease/disorders. Because the CLASP-5 gene is localized in the chromosome location 9p24.3, abnormal CLASP-5 gene regulation or deletion, rearrangement and/or mutations in CLASP-5 locus might be directly or indirectly associated with the onset of the listed diseases. Further, CLASP-5 gene can be used as a genetic probe to detect the abnormality in regions of these below listed genes and as a diagnostic marker for the related disease/disorders.

Please replace the paragraph beginning at page 110, line 13, with the following rewritten paragraph:

As shown in FIG. 2, a single band is clearly detected migrating at approximately 7.5kb in thymus, spleen kidney, placenta and peripheral blood lymphocytes in the Multiple Tissue Northern. Slight expression is detected in liver. In hematopoietic cell lines a similarly migrating band is detected in MV4-11 (myelomonocytic), HL-60 (myelocyte), and 9D10 (B-cell derived) cells.

Please replace the paragraph beginning at page 110, line 20, with the following rewritten paragraph:

BAC DNA was prepared from E. coli over night cultures using the QIAGEN DNA preparation system. All preps were performed according to the manufacturer's procedures, including the modifications for low copy number DNA

[illegible] corresponding to 20 microgram (μg) genomic DNA or 2 μg for BAC DNA were used for

restriction enzyme digests with Eco RI or HindIII (genomic DNA) or Eco RI and Pst I (BAC DNA). Digests were carried out in 150 microliter volume for 4 hours at 37°C. Digested DNA was ethanol precipitated and the pellet was resuspended in 20 microliter deionized water prior to migration over a 1.2 % agarose gel at 35 V over night. Running buffer was TAE, and the gel contained 0.1 g ethidium bromide/ml to visualize DNA.

Please replace the paragraph beginning at page 111, line 32, with the following rewritten paragraph:

CLASP proteins are described in commonly assigned Application Nos. 09/737,246; 09/136,969; 09/736,968; (all filed December 13, 2000), 60/240,508, 60/240,503, 60/240,539, 60/240,543 (all filed October 13, 2000); 09/547,276, 60/196,267, 60/196,527, 60/196,528, 60/196,460 (all filed April 11, 2000); 60/182,296 (filed February 14, 2000), 60/176,195 (filed January 14, 2000), 60/170,453 (filed December 13, 1999), 60/162,498 (filed October 29, 1999), 60/160,860 filed October 21, 1999, 60/129,171 filed April 14, 1999, and in published PCT publications PCT/US00/13161 (WO 00/69896); PCT/US00/13205 (WO 00/69898); PCT/US00/13166 (WO 00/69897); PCT/US00/10158 (WO 00/61747); and PCT/US99/22996 (WO 00/20434). The disclosures of each of the aforementioned applications and publications is expressly incorporated herein by reference in its entirety for all purposes.